HISTORY OF CATALYSIS AND ITS UTILITY IN SYSTEMIC PHTHISIS.

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I. HISTORY OF CATALYSIS.

THERE were many reactions in chemistry which were known to take place and were made use of, but why they took place in the way they did was not understood until catalytic action was recognized as the important factor.

Thus we have one-billionth part of soluble chromic chloride rendering insoluble chromic chloride soluble; a little platinum chloride enables us to dissolve tin in cold hydrochloric acid; a little potassium permanganate will render soluble many insoluble or difficultly soluble compounds.

We find in organic chemistry many catalyzers, or substances acting very similar to catalyzers, working a great many chemical changes more or less essential to our existence; hydrolyzing the starches to glucose and the proteins to amino acids, changing the nitrogen of the air to nitrites and nitrates, and many other chemical changes necessary for the continuance of life.

Next we learned that by means of high potentials we are able to divide many metals so finely that they may be suspended in liquids in such minute particles that they have the appearance of solutions and require the intervention of animal membrane to separate them. Such suspensions are called colloidal suspensions. Those of gold are ruby in color; those of platinum, brown, and those of silver, yellow. These suspensions have many of the properties of the catalyzers and enzymes. They will liberate oxygen from hydrogen peroxide. There are a number of chemicals which stop or restrain this catalytic and ferment action; such bodies as corrosive sublimate, cyanogen iodide, carbon monoxide and arsenic. These substances will restrain the action of ferments, catalyzers and colloidal solutions for some time. They are called paralyzers, and it should be noted that the most deadly paralyzers to these catalytic actions are the most dangerous paralyzers of plant and animal life. So it was thought, since ferment action which is similar to if not identical with catalytic action is so essential to life, that a study of catalyzers should lead to further knowledge in the study of the maintenance of life.

I want briefly here to call your attention to a few of the great many ways in which catalyzers are cheapening and simplifying processes in technical chemistry. These processes were called to my attention on a trip through New York and Chicago, and are not intended to be a complete list of the uses of catalyzers in chemical industries.

Hydrochloric acid is changed to chlorine and water by being passed over hot bricks impregnated with copper chloride. Hydrogen sulphide from soda-tank waste of a soda factory gives up its sulphur by presence of acid and iron oxide, or passing hydrogen sulphide into an area of hot chlorides of sodium and copper they obtained sulphate of sodium and chlorine gas. Roasted sulphur gas mixed with air scrubbed over a platinized washboard yielded in one year 800,000 tons of sulphuric acid. Naphthalene is generated from coal-tar acid oxidized by sulphuric acid in the presence of mercury and copper yielded indigo.

A solution of the peroxide of hydrogen and ether on the negative photographic plate gives an invisible positive; this followed with manganous sulphate gave a beautiful brown and alkaline solution giving a carbon print on the sensitized paper used. Ammonia from illuminating gas passed with air over platinum yielded nitric acid. Lead and manganese are used as driers for linseed oil. A series of zinc tubes through which vapors from alcohol were passed yielded eighty per cent aldehyde. At the packing plants the manipulation of fats with oleic acid in the presence of nickel yielded stearic acid; an enzyme from the castor bean was used to saponify the fats, yielding a soap that was lye free. So catalysis is playing an important part in the synthesis used by manufacturers and cheapens numerous products more or less necessary to our present method of living.

Catalysis has also been very useful to the biological chemists. Recently the nitrogen of the air has been combined with lime to form cyanamide of lime, in which form it may be used as a fertilizer.

Doctor Löhnis of Leipzig has been able to change "sarcosin" by means of cyanamide of lime and nitrogen to kreatin, an animal protein. So that we can have our meat manufactured by the aid of catalysis in the chemical laboratory.

Doctor Koch of Germany, about this time, developed the opsonian theory to explain certain phenomena observed in the blood. The white blood corpuscles absorb certain foreign substances as bacteria when found in the blood, and under certain conditions

will absorb them more readily than others. To prove this thesis to our own satisfaction we personally performed his experiment.

Segregated white blood corpuscles, exhaustively washed and plasma free, were maintained in a salt solution, and at body temperature, are indifferent to bacteria, but on the addition of blood plasma they consume their fill of the microbe life. This experiment proved one or the other of two things to be true: either there is something in the blood plasma that stimulates the white blood corpuscles or else the plasma must prepare the corpuscles so that they are ready to be absorbed. This suggested to the experimenter that the blood plasma must hold some catalytic agent toward the white blood corpuscle, the nucleus substance, which must prepare the microbe to be absorbed or taken up. We next discovered that a temperature of 65° C. annuls this microbe-destroying capacity. If, however, the microbes were incubated at a temperature approaching blood heat and the temperature then raised to 65° C., the corpuscles would take up the microbes. This indicates the opsonin to be a definite substance because it has a definite point of decomposition. From the observations of others coupled with those of our own we draw the following conclusions about opsonins:

(*a*) Opsonin will unite with dead innocuous microbes.

(*b*) This union will stimulate the body cells to produce more opsonin, in fact an excess of opsonin.

(*c*) The best agent to stimulate this action consists of the dead cells of that microbe which we are seeking to destroy.

(*d*) All bacilli stake their existence on the opsonian combat.

Doctor Koch in his experiments with tuberculosis along this line gave too large doses too close together, with unsatisfactory results. Doctor Wright by giving small doses was able to show that he could treat successfully many localized diseases by inoculating the menstra of the innocuous dead microbe cells. Since then, Doctor Wright and his assistants have been very busy supplying the demand for their opsonin.

Doctor Wright and his assistants did not understand the chemistry of the opsonin content and the albumen content of the excretions and the lesions of the tubercules. They said, "The lung tissue is filled with a substance which by chemical means exhibits albumen, salts, and nothing else that is characteristic."

The writer, as a result of his experiments, has reached the following conclusions:

(*a*) The opsonin content always contained nitrogen compounds of a high albuminous character.

(*b*) The albumen content of the phthisis-infected tissue is definite in its character. To determine just what it is and to change it to something soluble and nonparalyzing to the microbes is the secret of the solution in this opsonin battle.

(*c*) If the opsonin carrier and the morbid product stored in the cells by the bacteria can be changed into an inert (or better, into a nutrient), while passing the inoculation into the patient's system, we will thus fortify him against negative phases and make the dread tuberculosis bacillus the friend rather than the foe of its hosts.

The author has made a number of analyses of sputa and secretions from tubercular lesions. I have followed the methods described in the article, "Egg Albumen and Kindred Nitrogenous Compounds," thesis by Dr. S. J. Sammis of the University of Illinois, 1901–'02, on file in the library of that institution, and also used data compiled by Doctor Sammis in his albumen studies made under the auspices of the National Bureau of Animal Industry and published in his article "Cheese and Milk Products."

In these experiments we have used: (*a*) Internal sputa products, carefully collected by well-known scientists; (*b*) those from cultures on rabbits, guinea pigs and cats treated by the writer; (*c*) those submitted by others professionally interested.

For aid rendered in collecting the samples and the care taken in preservation and for the accurate history sent with samples, thanks are due to Dr. P. Anderson of California, to Prof. James Kinead, Doctors Ragsdal and Miller of Illinois, Dr. Jonathan Burrell and Dr. A. W. Palmer of St. Louis. For this aid, for samples so readily submitted, as well as advice and suggestions kindly offered from time to time, heartiest acknowledgment is hereby made. I also desire to thank the Rev. P. B. Peabody of Blue Rapids, Kan., for his aid in the proof-reading and transcribing of this report.

An examination, as given in the tables of the results attached, shows in one hundred and eighty-two samples out of two hundred tested with cyanamide of lime the conversion of the tubercular lesions into easily recognized alkali albuminates and easily absorbed casein, the presence of a definite base having been determined in the case of each sample.

Modern physical chemistry has, it would seem, caused us to burn all our old textbooks in chemistry and medicine. The indicated equations for reactions in chemistry were formerly set down as holding true *without fail*, "exceptions excluded." But when, at a later date, catalysis came to be known, it taught us why, in the ma-

jority of cases involving practical laboratory work, the actions theoretically indicated *did not occur.*

As long ago as the early eighties it was known to students, as a sort of marvel, that insoluble chromic chloride, when brought into the presence of a billionth part of the soluble chromic chloride, in water, became transformed in its nature, thus becoming soluble, like the latter salt. In those days we found that tin brought into contact with cold hydrochloric acid alone would yield us nothing. But we soon learned the trick of the master, and so, by the addition of a very small portion of platinum solution, presently had the metal dissolved. At a later date we were, in the quantitative laboratory, let into the secret of Fresenius, namely, that ever so small a portion of potassium permanganate would work the same miracle with almost all insoluble and "fractious" compounds.

In these determinations the strange thing of it all was this: the *catalyzing substance would remain, in every case, unaffected.* It could be used over and over again. Once initiated into the mysteries of the organic laboratory, we found that inorganic salts are not by any means the only catalytic substances. Microbes and bacteria we found to be the cause of all kinds of fermentations: the "yeast plant" causing sugar to change into alcohol; the "vinegar plant transforming alcohol into acetic acid; the "lactic ferment" changing sugar into lactic acid; "nitrous and nitric ferments" changing ammoniacal products into the nitrates of the soil. In all these cases the protoplasm of the organism had, in the presence of these compounds, wrought transfer without any change of the organic material. Diastase from barley malt, ptyalin from saliva, amplopepsin from pancreatic juice—all these we soon discovered to have the power of changing starch into sugar. Pepsin mingled with gastric juice would change insoluble albuminous forms into soluble forms, while rennet IN DIGESTO would work the miracle on 400,000 times its weight in the casein of milk.

Hardly had we become accustomed to thinking in terms of these last-named "enzymes" when we were introduced to the "colloidal suspensions." These, like the suspensions above noted as "solutions," required a membrane to separate the two elements. Incited by the wonder of these reactions, we set to work to make, for instance, the interesting platinum suspension, which is brown, in color. We then wrought out the ruby-colored suspension, of gold; the yellow one, of silver—performing these reactions at an electric plant where a high potential could be furnished. All these suspensions we found, when invited to determine them by means of

the ultra microscope, to be nothing more than finely divided metal solutions; that's all.

Further experiments with these suspensions proved them to have the same properties as do the vegetable and the animal enzymes, when brought into the field with certain other products. For example, both these enzyme types will cause peroxide of hydrogen to split up into water and oxygen gas. One gram of enzyme in 300,000,000 grams of water is found to be sufficient, when added to any quantity of peroxide, to affect the peroxide in the same way. In trying to control these apparent powers of the enzymes and colloidal suspensions we were to find that there are certain well-defined "paralyzers" for these agents in the inorganic field; such, for example, as corrosive sublimate, cyanogen iodide, carbon monoxide, arsenic—all of them agents that will restrain the activity of the enzyme or suspension for a definite time, after which the affected enzyme resumes its normal character. In the making of these studies it was emphatically noted that the most deadly paralyzers of these enzymes and colloidals, in their reactions on salts in solution, were also most dangerous paralyzers of the functions of animal and plant life. Straightway, then, the idea forced itself upon the thoughtful student that, since the enzymes are most intimately associated with the life of the cell, even more so than is the protoplasm, since the enzyme will work outside of the field of its producing protoplasm, and since these catalysts are in every nook and corner of the body—therefore the study of "the why" of the poisonous activity in question should lead to further knowledge in the study of the maintenance of life. In our investigations we were able, in spite of the subtle and complex form of the organism which produced the enzyme used, to produce artificially, by synthesis, a something that proved a counterpart of the enzyme. But, as to how it might become possible to eliminate or dispense with the poisonous paralyzers of the excretions after these had been used, "Aye, there (was) the rub."

The science of technology was at that time, however, forcing the attention of all true students upon itself; and we were having the idea dingdonged into our ears that there was a crying need in the field for experts who could unlock mysteries of commercial exploitation by the cheapening of processes. Then, forthwith, the startling information was sent percolating through our brains that the very catalytic reactions above detailed were now being depended upon to convert the raw dross material of the earth into the riches of the dream of the alchemist through the tense-nerved and tireless

intervention of the trained synthesist—that altruistic concomitant of every crying need.

Nor were proofs in any sense lacking. During a field trip to New York we saw hydrochloric acid passed over hot bricks that had heen impregnated with copper chloride; the acid came out as chlorine and water, while the bricks, with the saturant, were undisturbed. During the same week we were shown that hydrogen sulphide from the soda-tank "waste" of a soda factory was made to give up its valuable sulphur by simply passing the gas above named into the presence of acid and iron oxide. In like manner, by the passing of the hydrogen sulphide into an area of hot chlorides of sodium and copper, there were derived two valuable products, sulphate of sodium and chlorine gas. Shortly after, upon being introduced into the mysteries of a sulphuric-acid plant, we saw how roasted sulphur gas and air, passed over, and scrubbed upon, and dried upon, so to say, a platinized washboard, had produced that year 800,000 tons of sulphuric acid. Across the street an indigo factory, where naphthalene was generated from coal tar and afterwards oxidized by sulphuric acid in the presence of mercury and copper, was daily tolling off a poem more glorious than any sung by Keats or Byron—namely, a triumph-song of the achievements of man; a panegyric of his power to harness and master the forces of nature. Note, now, that even in this field the results attained were wholly due to this same subtle catalytic power of certain substances over other elements.

In our daily rounds of sight-seeing in the metropolis we found the photo-maker using this same faculty of well-known salts to cheat Old Sol out of his rights of performance. For within that artistic laboratory the cato-photo was no longer a dream, but a reality. Be well assured we jotted down, right then and there, memoranda of the germane formulæ processes: A solution of peroxide of hydrogen and ether on the negative photographic plate gave an invisible positive, by reason of the catalysis of the peroxide on the silver-sensitized surface. Thereafter, by the use of manganous sulphate, there was developed a beautiful brown tint, an alkaline solution giving a perfect "carbon print" on the sensitized paper used. On the return journey from New York even more of these catalytic marvels were seen. In a Chicago laboratory we observed the passing of ammonia from illuminating gas over platinum, with air; the ammonia presenting itself, at the end of this process, as nitric acid. Next in order, lead and manganese were found in use as driers of linseed oil. A zinc-tube series, through which vapors

of alcohol were passed, turned out 80 per cent aldehyde. Down at the packinghouses the manipulation of fats with oleic acid, in the presence of nickel resulted in that greatly useful by-product, stearic acid. An enzyme from the harmless castor bean was used in the saponifying of fats. The resultant consists of a soap that was lye-free, allowing the use of carbonates, at the very time when so stertorus a howl was going up about the detrimental effects of alkalies and arsenates in soaps.

While in Chicago we visited the general and experimental laboratories of chemistry in that great city. Here we found all experimenters at work upon some form or other of catalysis, the majority being on the *qui vive* for some process whereby the nitrogen of the air might be utilized in a number of ways to meet a number of imperative needs. Prominent among these needs was that of a soluble and efficacious fertilizer. Now note: hardly had the latter product been shown to be an indispensable factor in the cheapening of rations for mankind, when, upon our arrival at home, we saw the announcement that the great discovery had been made—cyanamide of lime, *ultima thule* of the aim of the alchemist, had recently been manufactured in Germany from atmospheric air.

Great are the contrasts in result wrought out by alchemy; and wide the range of its discovery-results: chemical odors so sweet as fairly to "shed a perfume on the violet," while at the opposite extreme is the awful nauseating whang of the torsin. Gunpowder has its triplet brothers, gun cotton and dynamite. Great is the sweep from the molding of the rubber dam of dental use to the wizard mystery of gold-extraction by cyanogen. And now all these, and other like discoveries of incalculable use to the human race, must give place, in point of marvel and utility, to the newly discovered nitrogen-of-the-air fertilizer.

But great as are the utilities already in sight, through this crucial discovery, in the stimulation and increase in the products of plant life, even more daring were the hopes that became speedily projected to the forefront of this discovery. Results more (literally) vital yet began to be anticipated, namely, even the metamorphosis of plant substance into the very muscle-cells of animals! Hardly had this projected hope begun to be discussed among chemic circles when, marvel of all marvels, there comes tripping over the heels of the former incredible bit of news the statement that the essential kreatin cells of cattle – real "extract of beef" – had just been made from beans and the kindred lentils of the vegetable world! Details of this discovery follow:

Doctor Löhnis, of Leipzig, had proved that certain bacteria that subsist upon nitrogen possess, by the catalytic action of their own excretions, the power of fixing the nitrogen of the air in the soil. Doctor Frank had produced cyanamide of lime from the nitrogen of the air, and he had demonstrated that when this cyanamide is brought into conjunction with sarcosin and air there is produced, by the catalytic action of the latter, the veritable flesh of animals — the cells, in fact, of extract of beef. This great achievement of the chemical catalytic transformation of vegetable into animal substance was announced in the terms of the following purely theoretical equation :

$$4\,C_3H_7O_2N + 5N + CaCN_2 = 3\,C_4H_2O_2N_3 + CaCN_2 + 2\,H_2O + 18H$$

Sarcosin + air + cyanamide = kreatin + cyanamide + water + hydrogen.

Astounding, indeed, is all this ; but why were we not to learn of some further development of this revolutionizing, potent catalysis, in that we have thus come the better to understand its laws.

II. CATALYSIS APPLIED TO THE MAN-LIFE.

Right at the above-indicated period physiological chemistry was following this perplexing theme of ours. By its light we were fast becoming aware that all of the body processes are no more, no less, than a series of well-developed catalytic actions. The theories of the leaders of our forerunners in physical chemistry were impregnated with the idea of the "opsonian" theory or hypothesis of the blood. Doctor Koch, of Germany, had developed this phase of experimentation ahead of any of the other chemists of his day. He had proved that white blood corpuscles have an appetite; that they do devour microbes when their appetite is keen. To prove this thesis to our own satisfaction we personally performed his suggested experiment, as follows:

Segregated white blood corpuscles, exhaustively washed and plasma-free, were maintained in a salt solution. It then developed, on experiment, that these corpuscles, even when raised to blood heat, are indifferent to bacteria. But upon the addition of blood-plasma they consume their fill of the microbe life. A process this of "benevolent assimilation."

The above experiment proved one or the other of two things to be true: either there is something in the blood-plasma that stimulates the white blood corpuscles, or else the plasma must prepare the microbes so that they are ready to be devoured.

Immediately, now, the thought was inwardly suggested to the experimenter that the blood-plasma must, in its effusions, hold out some catalytic agent toward the white corpuscle, the nucleus sub-

stance, which must prepare the microbe to be absorbed or taken up. This newly apprehended idea, in its possible relations with life, immediately added new stimulus and impetus to our study of physical chemistry. We now discovered by experiment that a temperature of 65° C. annuls this microbe-destroying capacity. If, however, it was found, the microbes were incubated at a temperature approaching blood heat, and the temperature then raised to 65° C., the corpuscles would devour the microbes. Thus was it clearly demonstrated that opsonin is a definite substance, because it has a definite point of decomposition.

Summarizing, now, the results just obtained with those already well known to those that had previously dealt with the subject, we now find the substance of the indicated facts and laws to be about as follows:

(*a*) Opsonin will unite with dead, innocuous microbes.

(*b*) This union will stimulate the body cells to produce more opsonin; in fact, an excess of opsonin.

(*c*) The best agent for the enhancing of this action consists of just the very cells of that microbe which we are seeking to destroy.

(*d*) All bacilli stake their existence on this opsonian combat.

III. RESULTS OF CATALYSIS UP TO A. D. 1900.

In the making of his corpuscle-plus-plasma-*versus*-microbe experiments, Doctor Koch gave fatal doses to his "patients," because unaware of the character of the phases produced, and ignorant of the fact that the bacilli which he was attacking with such perseverance were really aiming, in their work, at the achieving of a helpful product in the organisms which they were infecting. (This result they were, as we now know, unable to attain because of the excretive paralyzers produced in their work.)

At a later period Professor Wright proved beyond question that the successful treatment of any localized disease must consist in the inoculation of the *menstra* of the innocuous dead microbe cells themselves. But he did not understand the nature of that certain product toward which the tubercles were striving; nor did he realize that the tubercles were inhibited from carrying forward a helpful work for man by those very paralyzers which are an obstinate concomitant of their struggle—paralyzers that are always of a definite character, paralyzers which they are powerless to destroy.

In the pursuit of his experiments Professor Wright used doses of but the one-thousandth part of a milligram. Thus he was able to control all negative phases, and all phases of secondary occur-

rence (the flow-and-ebb phases of the opsonin treatment). On the other hand, Doctor Koch, in his studies, increased the negative phase of development by second inoculations, and his patients died. In other words, Doctor Koch had been striking out blindly, since he understood nothing as to the true rationale of the opsonin treatment. But since the successful issue of their experimental labors, Professor Wright and his assistants have been unable to find hours enough in both day and night for meeting the demands upon their clinical output. And yet they are unaware of the nature of that definite compound which is always produced by the phthisis microbe in human cells; and their work is thus hampered by their inability to spread the requisite information among medicos at large (a facilitation which, did they possess it, would enable physicians to assume the responsibility, or a share in it, for the inoculation processes). All physical chemists are agreed that the opsonin treatment, as a method of diagnosis, is a standard one; while yet, since this treatment stands without a "guard" or "aid" to assist the microbe in passing the so-called cheese-product-forming in phthisis, and the like substance-forming periods in other diseases, this inoculation lacks a vitally essential factor.

IV. A DEFINITE ALBUMIN CREATED BY TUBERCULAR BACILLI.

The experimenters of the decade just ended did not understand the chemistry of the problem under consideration. They were working from a "rule-of-thumb" process in all that pertained to the opsonin content and the albumin content of the excretions and the lesions of tubercles, in the case of phthisis and its allied forms in the human body. They therefore passed upon these elements and their phenomena in this manner: "The lung tissue is filled with a substance which, by chemical means, exhibits albumin, salts, and nothing else that is characteristic." Now, this is, from the writer's point of view, a very unscientific finding. Consequently the writer must now endeavor to establish, upon a reasonably secure basis, the verity and the applicability of the principles inwrought with the following discoveries which the writer has personally made:

(*a*) The opsonin content always contains nitrogen compounds of a high albuminous character.

(*b*) The albumin content of the phthisis-infected tissue is definite in its character. To discover this character and to accomplish the conversion of the albumin content into a substance potentially soluble and also nonparalyzing to the microbes which are (potentially) helpful in this eliminative work is the secret of the solution of this heretofore-described "opsonin battle."

(*c*) If we can convert the opsonin carrier and the morbid product stored in the cells of our patient into an inert (or, better, into a nutrient) albumin of higher or lower nitrogen content, while passing the inoculation into the patient's system, we shall thus fortify him, in the simple resulting reaction or catalytic transformation, against negative phases of development; and we shall thus make the dread tuberculosis bacillus the friend, rather than the deadly foe, of its host.

(*d*) We have already shown that by starting with the nonanimal product, sarcosin, we are able, by the introduction of the cyanamide of lime (nitrogen-of-the-air product), to change the sarcosin into kreatin—the veritable muscle, or flesh, tissue cells.

V. EXPERIMENTATION AND BIBLIOGRAPHIC REFERENCES.

Let us now try to show what we may further hope for in these directions, by the detailing of a few things that the writer has been learning in this domain through analytic work that has covered a period of several years. For details as to methods of separation and chemical determination of the albumins of sputa and lungular lesions herein tabulated, and for bibliographical references and a sample sterilization, the writer has followed the methods used as set forth in the article, "Egg Albumin and Kindred Nitrogenous Compounds," thesis, by Dr. S. J. Sammis, of the University of Illinois (1901–'02), on file in the library of that institution. He has also used further data since compiled by Doctor Sammis, in his albumin studies made under the auspices of the National Bureau of Animal Industry; the said studies being embodied in his article, "Cheese and Milk Products"—an article prepared by Doctor Sammis while he was located in the chemical laboratory at Madison, Wis. Sundry further addenda and variations, hereafter given, are the work of the present writer.

In our experiments we have used: (*a*) the internal sputa products of properly collected samples by well-known and reputable scientists; (*b*) those from cultures on rabbits, guinea pigs and cats treated by the writer; and (*c*) those that have been submitted by others that have been professionally interested. (The cultures on animals and those taken from human tissues have been properly sealed, hermetically, by the various bacteriologists and physicians that have so kindly assisted us in this tedious work. By consequence, these cultures, each with its own sample history attached, are guarded against the chance of serious error.)

For aid rendered in this important work thanks are due to Dr. P. Anderson, of California; to Prof. James Kinkead and Doctors Rags-

dale and Miller, of Illinois; and to Dr. Jonathan Burrill and Dr. A. W. Palmer, of St. Louis. (These are friends of our early student days; and for their aid in our investigations and for samples so readily submitted, as well as for advice and suggestions kindly offered from time to time, heartiest acknowledgment is hereby made.) I also desire publicly to thank Rev. P. B. Peabody, of Blue Rapids, Kan., for his aid in the proofreading and the transcribing of this report. This sort of aid is probably little appreciable by the average nonliterary layman; yet it is particularly acceptable to us, amid the stress of the finishing "strain" of this race.

An examination, as given in the tables of results attached, in 182 samples out of 200 intimately tested with this same cyanamide of lime, shows the conversion of the tubercular lesions into easily recognized alkali albuminates and easily absorbed casein, the presence of a definite base having been determined in the case of each sample. The series of changes thus far controlled were found to be as follows (empirically represented in series):

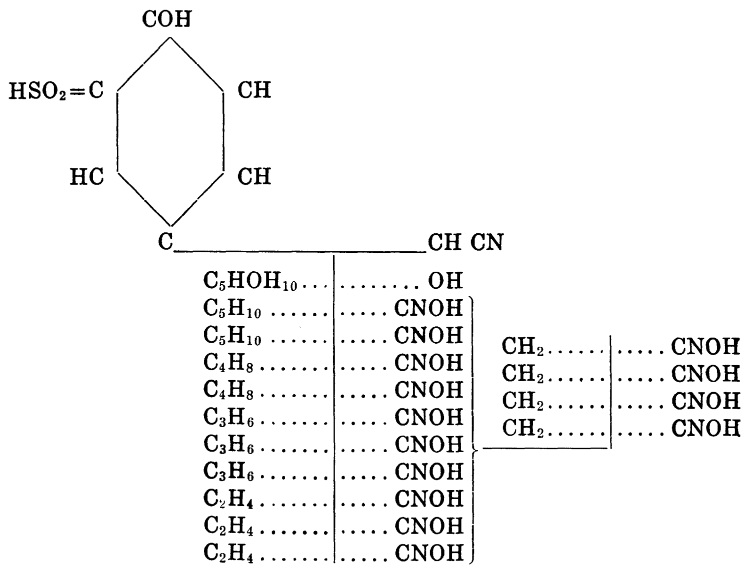
$C_4H_9N_3O_2$	Kreatin.
$C_4H_7N_3O$	Kreatinin.
$C_5H_4N_4O_2$	Xanthin.
$C_5H_{10}N_4O$	Xanthokreatinin.
$C_5H_4N_4O$	Hypoxanthin.
$C_7H_8N_4O_3$	Carnin.
$C_6H_{13}NO_2$	Leucin.
$C_9H_{11}NO_3$	Tyrosin.
$C_{11}H_4N_2O$	Urea.
$C_5H_4N_4O_3$	Uric acid.

The eleventh type of the above series, with sulphur and phosphorus (empirically represented), gives:

$C_{77}H_{120}N_{20}O_{26}$	Alkali albuminate.
$C_{144}H_{240}N_{40}S_2P_2$	Casein of milk.

VI. FORMULÆ AND DETERMINATIONS.

It may possibly be allowed to designate the formula of the molecule of the albumin-like substance "sarcosin," approaching as near to what it should be in structure as the imagination of man can possibly attain. I give the structural formula for sarcosin :



The soluble material then forms sarcosin; and gives with the product of CA C_2 plus 2N, or CA CN_2 plus C, = the kreatin or muscle-material; while it forms with the "lung-clog"--the casein—like material akin to cheese.

Content of Sputa and Lesions.

TABLE I. Percentage of Content of Affected Sputa.

The methods of determination herein followed were formulated by a modification of those laid down for "Content of Food Products," in Bulletin No. 108, U. S Department of Agriculture.

		Carbon.......	Hydrogen.....	Nitrogen.....	Sulphur.......	Oxygen.......	Phosphorus...	Total.........
CASE I.—Infant, 18 months old; lung phthisis; September, 1908.	I..........	61.02%	6.89%	13.68%	4.61%	10.71%	2.92%	99.83%
	II.........	61.25	6.80	12.90	5.00	10.25	2.90	99.10
	III........	61.03	6.87	13.52	4.75	9.97	2.85	99.09
	IV........	60.95	6.82	13.41	4.52	10.50	2.98	99.18
	V.........	61.53	6.75	13.52	4.60	10.70	2.95	100.05
	VI........	60.97	6.91	13.00	5.28	10.75	3.00	99.91
	VII.......	62.92	5.50	13.21	4.06	10.80	2.95	99.44
	VIII......	61.00	6.92	13.71	4.59	10.72	3.00	99.94
	IX........	60.45	6.42	14.01	4.60	10.78	2.90	99.16
	X.........	60.21	6.83	13.92	4.09	10.70	2.00	98 59
CASE II.—Lady, 38 years old; sputa collected at sanitarium; November, 1908.	I..........	61.09%	5.82%	12.68%	5.12%	10.75%	2.36%	98.72%
	II.........	61.75	6.82	12.99	5.00	10.91	2.85	100.32
	III........	61.50	6.66	13.65	4.52	10.81	2.98	100.12
	IV........	61.83	6.74	13.70	4.81	9.89	3.00	99.97
	V.........	61.71	5.98	13.71	4.61	10.71	2.98	99.76
	VI........	61.73	6.00	13.70	4.50	10.80	2.59	99.71
	VII.......	62.85	5.90	13.00	5.09	10.60	2.95	100.39
	VIII......	61.70	6.80	13 67	4.52	10.60	2.91	100.20
	IX........	61.09	6.89	13.50	4.55	10.70	2.90	99.63
CASE III.—Young lady, 19 years; galloping consumption; hospital, Topeka, November, 1908.	I..........	62.05%	6.09%	13.71%	4.02%	10.98%	3.00%	99.85%
	II.........	61.75	6.80	13.50	4.55	10.62	2.90	100.12
	III........	61.03	6.85	13.52	4.75	9.97	3.85	99.97
	IV........	61.09	6.80	13.75	4.59	10.71	2.92	99.86
	V.........	61.07	6.89	13.60	4.60	10.90	2.90	99.96
	VI........	61.92	6.97	12.71	4.65	10.75	3.00	100.00
	VII.......	61.95	6.81	13.66	4.72	10.09	2.98	100.21
	VIII......	61.07	6.98	13.09	4.95	10.81	2.95	99.85
	IX........	61.23	6.89	13.42	4.60	10.78	2.90	99.82
	X.........	62.21	6.90	12.00	4.72	10.80	2.95	99.58

		Per cent.			Per cent.
CASE IV.—Patient 39 years; average of 10 samples garcosin from urine in Bright's disease. September, 1908.	Carbon......	60.95	CASE X.—Amnitic fluid of tertiary stage; 15-months-old Belgian hare; 3 months pregnant; tuberculosis bacilli easily discerned.	Carbon......	62.00
	Hydrogen...	6.80		Hydrogen...	5.85
	Nitrogen....	12.92		Nitrogen....	13.80
	Sulphur.....	5.95		Sulphur.....	5.81
	Oxygen.....	10.45		Oxygen.....	10.33
	Phosphorus,	2.98		Phosphorus,	2.01
	Total.......	100.05		Total.......	99.80
CASE V.—Patient 50 years; average of 10 samples from knee exudations. October, 1908.	Carbon......	61.23	CASE XI.—Abortive case; fœtus and amniotic fluid in female, age 22 years, secondary stage; lesion determination. December, 1908.	Carbon......	61.90
	Hydrogen...	6.74		Hydrogen...	5.05
	Nitrogen....	13.70		Nitrogen....	13.09
	Sulphur.....	4.81		Sulphur.....	6.72
	Oxygen.....	9.89		Oxygen.....	10.59
	Phosphorus,	3.00		Phosphorus,	2.09
	Total.......	99.37		Total.......	99.44
CASE VI.—Patient 6 years; average of 10 analyses; systemic phthisis from birth. November, 1908.	Carbon......	61.70	CASE XII.—Negress, 29 years; systemic phthisis; sputa for 10 days; average of ten samples. October, 1909.	Carbon......	62.03
	Hydrogen...	6.80		Hydrogen...	5.05
	Nitrogen....	13.67		Nitrogen....	13.02
	Sulphur.....	4.52		Sulphur.....	5.91
	Oxygen.....	10.60		Oxygen.....	10.76
	Phosphorus,	2.91		Phosphorus,	2.98
	Total.	100.20		Total.......	99.75
CASE VII.—Patient 34 years; ten determinations; amniotic fluid of mother in sixth month of pregnancy. December, 1908.	Carbon......	62.05	CASE XIII.—From cadaver (phthisic patient) at time of embalming, 4 hours after death. October, 1909.	Carbon......	60.98
	Hydrogen...	5.09		Hydrogen...	6.11
	Nitrogen....	13.60		Nitrogen....	13.05
	Sulphur.....	5.55		Sulphur.....	5.82
	Oxygen.....	10.62		Oxygen.....	10.70
	Phosphorus,	2.90		Phosphorus,	2.99
	Total.......	99.81		Total.......	99.65
CASE VIII.—Patient 42 years; systemic phthisis; laborer in gypsum mills; secondary stage. January, 1909.	Carbon......	61.01	CASE XV.—Guinea pig, 18 months old; fresh sputa; 90 days of tubercular affection produced by inoculations with tubercular bacilli. October, 1909.	Carbon......	61.90
	Hydrogen...	5.83		Hydrogen...	4.96
	Nitrogen....	13.71		Nitrogen....	13.71
	Sulphur.....	5.86		Sulphur.....	6.55
	Oxygen.....	10.60		Oxygen.....	10.93
	Phosphorus,	2.90		Phosphorus,	2.05
	Total.......	99.91		Total.......	100.10
CASE IX.—Patient 12 years; case hydrocephalous expectorations of tertiary phthisis. January, 1909.	Carbon......	61.21	CASE XVI.—Amniotic fluid; lesions of female greyhound; inoculation 33 days with tubercular bacilli; age 14 months.	Carbon......	....
	Hydrogen...	6.07		Hydrogen...	....
	Nitrogen....	13.72		Nitrogen....	....
	Sulphur.....	6.82		Sulphur.....	....
	Oxygen.....	10.62		Oxygen.....	....
	Phosphorus,	2.95		Phosphorus,	....
	Total.......	101.39		Total.......	....

REMARKS.

Cases IV, VII and XIII were samples with direct view to arrive at molecular weight of "garcosin."

Cases V, IX and XIII, special studies to determine whether a definite material was present.

Cases VI, X and XV are typical, and content of amniotic fluid was ultimately determined and published first in S. Ill. Med. Jour., 1897.

Cases VII, XI and XVI are in the nature of corroborative evidence.

VII. STUDIES IN AN ANTITOXIN ELIXIR, OR CARRIER, FOR CALCIUM CYANAMIDE.

USE OF $CaCN_2$ IN THE FURTHERING OF THAT CHEMICAL TRANSFORMATION, OR CATALYSIS' WHICH THE TUBERCULAR BACILLUS FAILS, BECAUSE OF THE SHORTNESS OF ITS LIFE' TO COMPLETE.

An elixir which performs the functions of a carrier for cyanamide of lime, in the case of minimum doses, without salivation effects, is the following:

℞—Calcium glycerophosphate, 8 gr.
Sodium glycerophosphate, 16 gr.
Iron glycerophosphate, 1½ gr.
Manganese glycerophosphate, 1 gr.
Quinine glycerophosphate ½ gr.
Aromatic elixir of cascara sagrada *q.s.* to make 1 pint.
Macerate in the above $\frac{1}{60}$ gr. of calcium cyanamide, pulv.
Sig.—Give 60 mm. three times daily, according to patient's needs, with hypodermic.

The foregoing elixir was used in the treatment of animals with cyanamide of calcium.

VIII. ACTION OF ELIXIR ON ANIMALS.

Two dozen guinea pigs of the healthiest type inoculated for a period of twenty-five to ninety days, in due course, with tubercules; were given hypodermically the foregoing formula for first five days, also internally, the said elixir, and all are healthy and to all appearances fat and well.

Cows with tubercular bacilli were given, hypodermically, the foregoing formula for the first five days; also internally. All are healthy, and, to all appearances, fat and well, gaining each day. The same is true of twelve infected Belgian hares infected to tertiary stage, there not having been a single one of them that did not recover fully in 171 days.

IX. HOPES AND CONCLUSIONS BASED UPON THIS INVESTIGATION.

We gather, therefore, from these studies—

First: That there is a definite organic basis to the exudations of the tubercular bacillus.

Second: That this organic basis is an analogue to the base of milk, known as casein.

Third: That it is possible to attack in animals that are physiologically similar to man the artificially produced systemic phthisis state (even after the subjects have reached the most direful pathological condition, after inoculation with tubercules), with success.

Fourth: That we have been in many cases more successful in the combating of the artificially induced disease than in the propagation of cultures of bacilli.

Fifth: That the comparative study of certain cancerous effluvia or deposits, due to poisoning with fish fins, has revealed lesions closely analogous in basis to the sputa albumin of tubercular bacillus growths.

Sixth: That a carrier, or elixir, has been made which will successfully convey the deadly cyanamide of lime into and out of the human system, producing in its passage the desired catalytic action. (This, thus far inferentially, from analogous success with animals physiologically similar to man.)

Pregnant evidence of success is on the side of the experimentation which we have carried on during the past nine years. If it thus becomes possible to transform the sad-eyed patient, awaiting sealed doom, into a healthy being, radiant with life joy, the cup of this writer will run over and over. And surely we are now on the right road to reach ultimately the long-sought end. As ever, that end will be found, whenever it shall be found, in the laboratory of the skilled enthusiast. And the final, comprehensive solution of the long baffling and ultra-complex tuberculosis problem will mean unparalleled boon of physical well-being for human kind, involving results that superabound in mercy shown, in gladness unspeakable attained.

ADDENDA.

During this year of grace 1910 the writer has had the pleasure of trying the virtue of the catalytic action of this now famous cyanamide of lime from coast to coast in America. Friends, surgeons of the Red Cross Society, have day by day found patients who were willing to submit to inoculation with cyanamide elixir. Here in the white-walled city of Manila, P. I., have been discharged five children of the first families of the Luzon island, pronounced cured, the same having been originally possessed of variant forms of tuberculosis in the several stages of development. To see some of these playing child games, further, to see of an evening the half-dozen young men, sixteen weeks ago in all but hopeless condition with tuberculosis, now apparently hale and hearty, playing tennis and indoor base ball, is the crowning joy of this long-drawn-out period of experimentation. Added to their number appears upon the roster of the cured, in all parts of the United States, the writer's friends made glad to the number of fifty-five; and the writer awaits with anxiety the development of a manufactory for production of materials, that no delay may further be necessary, and to give to his beloved Academy in the Sunflower state, U. S. A., the results herein set forth.